

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

PCT Application
PCT/JP2003/007407



Rec'd PCT/PTO

9 MAR 2006

Applicant's or agent's file reference	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP03/07407	International filing date (day/month/year) 11 June 2003 (11.06.03)	Priority date (day/month/year)
International Patent Classification (IPC) or national classification and IPC C12N 15/09, 1/21, C12P 17/18 //(C12N 1/21, C12R1:465) (C12P17/18, C12R1:465)		
Applicant THE KITASATO INSTITUTE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 11 July 2003 (11.07.03)	Date of completion of this report 05 November 2003 (05.11.2003)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP03/07407

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed
- ☐ the description:
 pages _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☐ the claims:
 pages _____, as originally filed
 pages _____, as amended (together with any statement under Article 19
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☐ the drawings:
 pages _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____
- ☐ the sequence listing part of the description:
 pages _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	1-15	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-15	NO
Industrial applicability (IA)	Claims	1-15	YES
	Claims		NO

2. Citations and explanations

Document 1: WO 93/18779 A1 (MERCK & CO., INC.) September 30, 1993
Document 2: J. Antibiot. 1991, Vol. 44, No. 2, p. 232-240
Document 3: J. Antibiot. 1988, Vol. 41, No. 4, p. 519-529
Document 4: Protein, Nucleic Acid and Enzyme, Vol. 43, No. 9 (1998), p. 1265-1277
Document 5: Kagaku to Seibutsu, Vol. 34, No. 11 (1996), p. 761-771
Document 6: Bioscience & Industry, Vol. 59, No. 8 (2001), p. 530-533
Document 7: JP 2003-33188 A (Kyowa Hakko Kogyo Co., Ltd.) February 4, 2003
Document 8: Ind. Microorg. (Edited by BALTZ R.H. et al.) 1993, p. 245-256

Claims 1, 3, 5 and 6

Based on the descriptions in documents 1 and 2 cited in the international search report, the inventions of claims 1, 3, 5, and 6 lack an inventive step.

Documents 1 and 2 describe a process for glycosylation or hydroxylation of position 13 of nemadictin (LL-F28249 α) using microorganisms belonging to the genus *Streptomyces*. Persons skilled in the art can easily obtain other microorganisms belonging to the genus *Streptomyces* that perform glycosylation or hydroxylation at position 13 of nemadictin.

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V:

Claims 1-15

Based on the descriptions in documents 2-8 cited in the international search report, the inventions of claims 1-15 lack an inventive step.

Document 3 describes a process for producing nemadictin using *Streptomyces cyaneogriseus* sp. noncyanogenus.

As described in documents 4 and 5, in the synthesis of polyketide compounds typified by avermectins, this examination finds that modification of the synthetic pathway and regulation of that modification by the combination of various species of the biosynthetic enzymes (polyketide synthases: PKSs) thereof (i.e., hybrid PKSs) were widely performed before the filing date of this application.

Documents 5 and 6 describe using the genes of the biosynthetic enzyme for nemadictin, which belongs to the same family, in the production of modified forms of avermectins. Document 7 states that in the enzymes that synthesize avermectins and nemadictin, a specific enzyme (ER) determines whether or not there is an oxygen atom at position 13 (ER is not present in avermectins, which has an oxygen at position 13, and ER is present in nemadictin, which does not have an oxygen at position 13).

In light of the above descriptions, this examination finds that in the process for producing nemadictin using the *Streptomyces cyaneogriseus* sp. noncyanogenus described in document 3, persons skilled in the art can easily focus on glycosylation at position 13, prepare a hybrid PKS using the genes of the biosynthetic enzymes for avermectins, which belong to the same family as nemadictin, and at that time modify that biosynthetic pathway so that ER, which determines whether or not an oxygen atom is at position 13, is not present.